

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
Rainer BISCHOFF et al.)
Application No.: Unassigned) Group Art Unit: Unassigned
(Continuation of Serial)
No. 09/171,845) Examiner: Unassigned
Filed: December 18, 2001)
For: NOVEL LIPID COMPOUNDS AND)
COMPOSITIONS CONTAINING)
SAME USED FOR)
THE TRANSFER OF AT LEAST AN)
ACTIVE SUBSTANCE, IN)
PARTICULAR A POLYNUCLEOTIDE)
INTO A TARGET CELL AND)
THERAPEUTIC USE)

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination on the merits, please amend the above-identified application as follows:

IN THE SPECIFICATION:

After the title of the application on page 1, please insert the following paragraph:

--This application is a continuation of U.S. Application Serial No. 09/171,845, filed on October 28, 1998, which is a national stage filing under 35 U.S.C. § 371 of

International Application No. PCT/FR98/00389, filed on February 27, 1998, which
International Application was not published by the International Bureau in English on
September 3, 1998.--

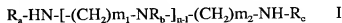
IN THE CLAIMS:

Please cancel claim 1, without prejudice or disclaimer to the subject matter
disclosed therein.

Please add new claims 45-59 as follows:

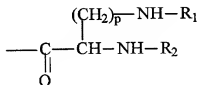
--45. A pharmaceutical preparation comprising an effective amount of at least one
complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

the R_a , R_b and R_c residues are, independently of each other, a hydrogen atom or a
group of formula II:



with:

R_1 and R_2 are, independently of each other, C_6-C_{23} alkyl or alkenyl radicals, which are linear or branched, or radicals $-C(=O)-(C_6-C_{23})$ alkyl or $-C(=O)-(C_6-C_{23})$ alkenyl, which are linear or branched, aryl radicals, cycloalkyl radicals, fluoroalkyl radicals, polyethylene glycol groups, oxyethylene or oxymethylene groups, with the proviso that when one of the R_1 or R_2 is a polyethylene glycol group, an oxyethylene or an oxymethylene group, the other is a linear or branched C_6-C_{23} alkyl or alkenyl radical, a linear or branched $-C(=O)-(C_6-C_{23})$ alkyl or $-C(=O)-(C_6-C_{23})$ alkenyl radical, an aryl radical, a cycloalkyl radical, a fluoroalkyl radical,

p is a positive integer from 1 to 4,

n is a positive integer from 1 to 6,

m_1 and m_2 are a positive integer from 1 to 6, and m_l may be different for each motif $-(CH_2)_{m_l}-NR_b$, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

(ii) at least one active substance comprising at least one negative charge; and

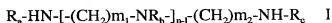
(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance;
in combination with a pharmaceutically acceptable carrier.

46. The preparation of claim 45, comprising, in addition, at least one adjuvant which enhances the introduction of the active substance, comprised in said complex, into a cell.

47. The preparation of claim 46, wherein said adjuvant comprises chloroquine, a protic polar compound chosen from propylene glycol, polyethylene glycol, glycerol, ethanol, 1-methyl-L-2-pyrrolidone or derivatives thereof, or an aprotic polar compound chosen from dimethyl sulfoxide (DMSO), diethyl sulfoxide, di-n-propyl sulfoxide, dimethyl sulfone, sulfolane, dimethylformamide, dimethylacetamide, tetramethylurea, acetonitrile.

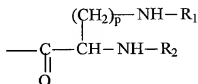
48. A method for enhancing expression of a gene in vivo wherein said method comprises the step of administering to a body a complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

the R_a , R_b and R_c residues are, independently of each other, a hydrogen atom or a group of formula II:



with:

R_1 and R_2 are, independently of each other, $C_6\text{-C}_{23}$ alkyl or alkenyl radicals, which are linear or branched, or radicals $\text{-C(=O)-(C}_6\text{-C}_{23})$ alkyl or $\text{-C(=O)-(C}_6\text{-C}_{23})$ alkenyl,

which are linear or branched, aryl radicals, cycloalkyl radicals, fluoroalkyl radicals, polyethylene glycol groups, oxyethylene or oxymethylene groups, with the proviso that when one of the R_1 or R_2 is a polyethylene glycol group, an oxyethylene or an oxymethylene group, the other is a linear or branched C_6-C_{23} alkyl or alkenyl radical, a linear or branched $-C(=O)-(C_6-C_{23})$ alkyl or $-C(=O)-(C_6-C_{23})$ alkenyl radical, an aryl radical, a cycloalkyl radical, a fluoroalkyl radical,

p is a positive integer from 1 to 4,

n is a positive integer from 1 to 6,

m_1 and m_2 are a positive integer from 1 to 6, and m_l may be different for each motif

$-(CH_2)_{m_1}-NR_b$, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

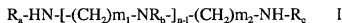
(ii) at least one active substance comprising at least one negative charge; and

(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance,

wherein said complex comprises a gene and wherein said gene is transferred into a cell and expressed by said cell.

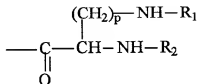
49. A method for enhancing expression of a gene in vivo wherein said method comprises the step of administering to a body a complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

the R_a , R_b and R_c residues are, independently of each other, a hydrogen atom or a group of formula II:



with:

R_1 and R_2 are, independently of each other, $C_6\text{--}C_{23}$ alkyl or alkenyl radicals, which are linear or branched, or radicals $\text{—C(=O)—(C}_6\text{--}C_{23})$ alkyl or $\text{—C(=O)—(C}_6\text{--}C_{23})$ alkenyl, which are linear or branched, aryl radicals, cycloalkyl radicals, fluoroalkyl radicals, polyethylene glycol groups, oxyethylene or oxymethylene groups, with the proviso that when one of the R_1 or R_2 is a polyethylene glycol group, an oxyethylene or an oxymethylene group, the other is a linear or branched $C_6\text{--}C_{23}$ alkyl or alkenyl radical, a linear or branched $\text{—C(=O)—(C}_6\text{--}C_{23})$ alkyl or $\text{—C(=O)—(C}_6\text{--}C_{23})$ alkenyl radical, an aryl radical, a cycloalkyl radical, a fluoroalkyl radical,

p is a positive integer from 1 to 4,

n is a positive integer from 1 to 6,

m_1 and m_2 are a positive integer from 1 to 6, and m_l may be different for each motif $\text{—(CH}_2\text{)}_{m_l}\text{—NR}_b$, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

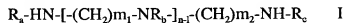
(ii) at least one nucleic acid comprising a gene of interest and elements allowing for the expression of said gene of interest; and

(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance,

wherein said gene is transferred into a cell and expressed by said cell.

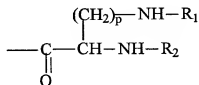
50. A method for enhancing expression of a gene in vivo wherein said method comprises the step of administering to a body a complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

R_a and R_b are hydrogen atoms, R_c is a group of formula II:



with:

R_1 and R_2 are identical and are radicals $-C(=O)-(C_6-C_{23})$ alkyl or $-C(=O)-(C_6-C_{23})$ alkenyl, which are linear or branched,

p is 1,

n is 2,

m_1 is 4 and m_2 is 3, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

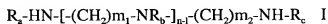
(ii) at least one nucleic acid; and

(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance,

wherein said complex comprises a gene and wherein said gene is transferred into a cell and expressed by said cell.

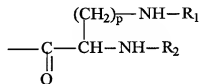
51. A method for enhancing expression of a gene in vivo wherein said method comprises the step of administering to a body a complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

R_a and R_b are hydrogen atoms and R_c is a group of formula II:



with:

R_1 and R_2 are identical and are chosen from stearoyl or oleoyl radicals,

p is 1,

n is 2,

m_1 is 4 and m_2 is 3, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

(ii) at least one nucleic acid; and

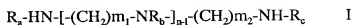
(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance;

in combination with a pharmaceutically acceptable carrier,

wherein said complex comprises a gene and wherein said gene is transferred into a cell and expressed by said cell.

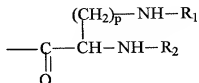
52. A method for enhancing expression of a gene in vivo wherein said method comprises the step of administering to a body a complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

R_a and R_c are hydrogen atoms and R_b is a group of the formula II:



with:

R_1 and R_2 are identical and are chosen from the radicals $-C(=O)-(C_6-C_{23})$ alkyl or $-C(=O)-(C_6-C_{23})$ alkenyl, which are linear or branched,

p is 1,

n is 2,

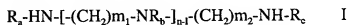
m_1 is 4 and m_2 is 3, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

(ii) at least one nucleic acid; and

(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance;
in combination with a pharmaceutically acceptable carrier, wherein said complex comprises a gene and wherein said gene is transferred into a cell and expressed by said cell.

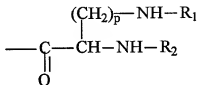
53. A method for enhancing expression of a gene in vivo wherein said method comprises the step of administering to a body a complex, wherein said complex comprises:

(i) at least one compound of the formula:



wherein:

the R_a and R_c are each hydrogen atoms, and R_b is a group of formula II:



with:

R_1 and R_2 are identical and chosen from stearyl or oleoyl radicals,

p is 1,

n is 2,

m_1 is 4 and m_2 is 3, and wherein the total number of groups of formula II in said compound is between 1 and 4, wherein said compound is a cationic compound;

(ii) at least one nucleic acid; and

(iii) at least one adjuvant which enhances the formation of the complex between said compound and said active substance;
in combination with a pharmaceutically acceptable carrier, wherein said complex comprises a gene and wherein said gene is transferred into a cell and expressed by said cell.

54. The method of claim 48, wherein said complex is administered by intramuscular injection, by inhalation, by intratracheal injection, by instillation, through the use of an aerosol, by the topical route or by the oral route.

55. The method of claim 49, wherein said complex is administered by intramuscular injection, by inhalation, by intratracheal injection, by instillation, through the use of an aerosol, by the topical route or by the oral route.

56. The method of claim 50, wherein said complex is administered by intramuscular injection, by inhalation, by intratracheal injection, by instillation, through the use of an aerosol, by the topical route or by the oral route.

57. The method of claim 51, wherein said complex is administered by intramuscular injection, by inhalation, by intratracheal injection, by instillation, through the use of an aerosol, by the topical route or by the oral route.

58. The method of claim 52, wherein said complex is administered by intramuscular injection, by inhalation, by intratracheal injection, by instillation, through the use of an aerosol, by the topical route or by the oral route.

59. The method of claim 53, wherein said complex is administered by intramuscular injection, by inhalation, by intratracheal injection, by instillation, through the use of an aerosol, by the topical route or by the oral route.--

REMARKS

Entry of the foregoing and favorable consideration of the subject application, in light of the following remarks, are respectfully requested.

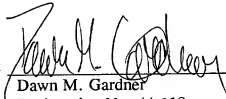
By the foregoing amendment, the specification has been amended to update the status of the copending applications to which this application claims benefit of priority pursuant to 37 C.F.R. § 1.78(a)(2), and the addition of an indication that the international application to which this application claims benefit of priority was not published under PCT Article 21(2) in English. Furthermore, new claims 45-59 have been added. New claim 45 finds support on page 36, line 11, of the specification as filed. New claim 46 finds support in claim 41 as originally filed. New claim 47 finds support in claim 42 as originally filed. New claims 48-59 find support on page 36, line 11, and throughout the specification as filed. No new matter has been added by the present amendment.

In the event that there are any questions relating to this Preliminary Amendment, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: December 19, 2001